REMARKS

Claims 1-8 are rejected. Claims 1, 3 and 4 have been amended. Claim 2 has been canceled. Claims 1 and 3-8 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

The basis for the amendments to claim 1 can be found in claim 2 as originally filed, Fig. 2 and on page 7, lines 7-10 of the specification as originally filed.

Rejection of Claims 1-6 Under 35 U.S.C. §102(b):

In Section 3 of the Office Action dated September 25, 2006, the Examiner has rejected claims 1-6 under 35 U.S.C. §102(b) as being anticipated by Bensimon et al. (hereinafter referred to as "Bensimon," U.S. Patent 6,054,327, 102(b) date 04/25/2000).

The Examiner indicates that several aspects of the instant claim 1 have been broadly interpreted. The Examiner interprets passing the hybridized DNA complex "from a reservoir in a microfluidic device" as moving any portion of the hybridized DNA complex initially in a holding area in a device designed to contain small amounts of liquids. The Examiner interprets passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel" as moving any portion of the hybridized DNA complex through a small passageway that involves an acceleration of flow through the passageway.

The Examiner indicates that Bensimon teaches a method of analyzing DNA comprising hybridizing the DNA in solution with probes having fluorescent reagents and then detecting the position of the probes after aligning the DNA. The Examiner states that Bensimon also teaches that DNA molecules placed in a channel between cover slips can be aligned by the evaporation flow parallel to a moving meniscus in the channel. The Examiner interprets this as being in a "reservoir in a microfluidic device." The Examiner further interprets that as the meniscus initially moves through the channel between the cover slips, there will be an acceleration of fluid flow in the channel and a portion of the DNA complex will pass through the channel as it extends to a linear configuration as passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel, thereby causing said hybridized DNA

complex to extend into a substantially linear configuration." The Examiner states that the probes used to hybridize DNA can be oligonucleotides, RNA, DNA, and peptide nucleic acids and that oligonucleotide probes can be labeled with fluorescent labels and microbeads. The Examiner interprets the recitation "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,..." as detecting one or more optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex. The Examiner states that Bensimon teaches the analysis of the entire length of a linear labeled nucleic acid molecule which allows for determining the sequential order of labels on the target, and specifically teaches the use of multiple probes to determine the position or size of multiple specific sequences, which is identification of the target DNA molecule. The Examiner has misconstrued the claims and the rejection is respectfully urged as in error.

Bensimon discloses a method for aligning macromolecules such as polymers or macromolecules with biological activity, especially DNA, or proteins and also relates to the application of this method in processes for detecting, for measuring intramolecular distance, for separating and/or for assaying a macromolecule in a sample. Macromolecules such as nucleic acids, proteins, lipids or polysaccharides are aligned on a support surface by passing the macromolecules through a meniscus of a solvent containing the macromolecules. The meniscus may be that of a solvent between two surfaces at an interface of the solvent with air. One end of a macromolecule is attached to one surface which may be a glass surface and another end is free. The meniscus is moved relative to the surface to which the end is attached such as by evaporating the solvent or by moving the surface. As the macromolecule passes through the meniscus, the macromolecule aligns on the surface perpendicular to the meniscus. This method may be used in assaying, measuring intramolecular distance and/or separating of macromolecules.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA

molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of the target molecule to identify the target DNA molecule from its DNA sequence.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. Claim 1 reads "passing said hybridized DNA complex in a random coil state in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" MPEP 2111.01 states that "the words of a claim must be given their "plain meaning" unless they are defined in the specification." This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); Chef America, Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004) (Ordinary, simple English words whose meaning is clear and unquestionable, absent any indication that their use in a particular context changes their meaning, are construed to mean exactly what they say. Thus, "heating the resulting batter-coated dough to a temperature in the range of about 400oF to 850oF" required heating the dough, rather than the air inside an oven, to the specified temperature.). Merriam-Webster Online Dictionary defines the term "through" to mean *"(1) -- used as a function word to indicate movement into at one side or point and out at another and especially the opposite side of <drove a nail through the board> (2): by way of <left through the door> (3) -- used as a function word to indicate passage from one end or boundary to another <a highway through the forest> <a road through the desert> (4): without stopping*

for: PAST <drove through a red light> b -- used as a function word to indicate passage into and out of a treatment, handling, or process <the matter has already passed through her hands>". Cambridge on-line dictionaries define the term "through" to mean: "*from one end or side of something to the other, as in "They walked slowly through the woods." Or "We drove through the tunnel.*"" The Compact Oxford English Dictionary defines "through" to mean: "moving in one side and out of the other side of (an opening or location)." Thus, the plain meaning of the term indicates that the hybridized DNA complex proceeds in one side of the channel and out the other. In addition, MPEP 2111.01 continues that ""Plain meaning" refers to the ordinary and customary meaning given to the term by those of ordinary skill in the art" and "It is the use of the words in the context of the written description and customarily by those skilled in the relevant art that accurately reflects both the "ordinary" and the "customary" meaning of the terms in the claims. Ferguson Beauregard/Logic Controls v. Mega Systems, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003) (Dictionary definitions were used to determine the ordinary and customary meaning of the words "normal" and "predetermine" to those skilled in the art. In construing claim terms, the general meanings gleaned from reference sources, such as dictionaries, must always be compared against the use of the terms in context, and the intrinsic record must always be consulted to identify which of the different possible dictionary meanings is most consistent with the use of the words by the inventor.)." Additionally, the specification supports the definition of "through" as the movement of the hybridized DNA complex in one side of the channel and out the other side of the channel. See Fig. 1a and 1c (A, B, C, D, E, F).

The Examiner broadly interprets the meaning of passing a hybridized DNA complex through the channel. The plain wording of claim 1 indicates that the "hybridized DNA complex" passes through the channel. Claim 1 does not read "part of the hybridized DNA complex" or "the hybridized DNA complex and any part thereof." The normal reading of the claim indicates that the entire complex passes through the channel. Reading the claim as referring to only a part of the complex is contrary to customary usage. Figs. 1a and 1c further clarify that the entire complex passes through the channel. Fig. 1a (F) is located outside the exit of the narrow channel. Referring to Fig. 1c, it is clear from (F) that the entire molecule passes through the channel. The Examiner also indicates

that Claim 1 does not recite any limitations with regard to how much of the DNA complex is passed through the channel and therefore movement of all but the fixed end of the DNA complex through the area between the plates as taught by Bensimon in Fig. 6 can be reasonably interpreted as passing the DNA complex through a narrow channel. As discussed above, the term "through" in claim 1 refers to movement of the hybridized DNA complex in one side and out the other of the channel. Bensimon makes no such disclosure. Also comparison of Fig. 6 of Bensimon to Fig. 1a of the present invention would clearly indicate the differences between Bensimon and the present invention.

OneLook® Dictionary at www.onelook.com defines the term "channel" to mean "a passage for water (or other fluids) to flow through" and "reservoir" to mean, "tank used for collecting and storing a liquid (as water or oil)." According to MPEP 2111.01 as discussed above, these terms should be given their common meaning. This meaning is also supported in the specification by Figs. 1a and 1b, which make clear that the reservoir and channel are two distinct parts of the microfluidic device. Review of Bensimon Fig. 6 indicates that there are not two separate and distinct parts of the device through which a portion of the hybridized complex passes. The reference teaches only a single tube and makes no distinction between a reservoir and a narrow channel as claimed by the instant invention.

Therefore, as Bensimon fails to disclose the passage of a hybridized complex from a reservoir and through a narrow channel, Bensimon fails to anticipate the present claims and Applicants request that the Examiner reconsider and withdraw the rejection.

In Section 4 of the Office Action dated September 25, 2006, the Examiner indicates that the other provided definitions for the term "through" are less definitive regarding passage of an element out of a defined area. For example the Merriam-Webster definition 3 indicates only "passage from one end or boundary to another", and the Cambridge online definition indicates only "from one end or side of something to the other". The Examiner asserts that the plain meaning of the term "through" does not require passage of the element out of the confines of the required area, but only requires some movement within the defined area. The Examiner states that while the Remarks indicate that the specification supports the definition of "through" as the movement in one side and out the other

and points to Fig 1 a and 1 c, and that the figures indicate that the whole hybridized DNA complex passes in one end of a channel and out the other, the indicated figures may be considered exemplary as they do not assign any definitions to the terms "through" or "hybridized DNA complex" that are required for the claims. The Examiner maintains that the claims do not recite any limitations with regard to how much of the DNA complex is passed through the channel and therefore movement of all but the fixed end of the DNA complex through the area between the plates as taught by Bensimon in Fig. 6 can be reasonably interpreted as passing the DNA complex through a narrow channel. With regard to the channel and reservoir being distinct features the Examiner states that the figures do not assign any definitions required by the terms recited in the claims. The Examiner maintains that the claims recite the terms "reservoir" and "channel" only as named parts of a microfluidic device with no structural limitations or particular spatial relationship regarding either a "reservoir" or a "channel." Applicants maintain that the rejection is in error.

Examiner indicates that the term "through" only requires some movement within a defined area. However, this conclusion is incorrectly drawn from the citations. Even taking the less applicable definition of through as stated in Merriam-Webster definition 3 or the Cambridge online definition the term through at least requires movement from one boundary or end to another, not merely any movement within a defined area as suggested by the Examiner. The example cited in Merriam-Webster is a highway through the forest, which indicates moving from at least one end of the forest to the other, not a highway that begins and ends in the forest without reaching the boundaries of the forest. Bensimon does not teach moving a hybridized complex from one boundary to another. As shown in Bensimon Fig. 6, one end of the complex is affixed to a wall and makes no movement, and therefore clearly does not move through a narrow channel as claimed by the instant invention. The free end of the hybridized complex begins in a random state and is stretched within the area between the plates and not from one boundary to the other. Bensimon fails to teach moving a hybridized complex from one boundary to another, much less into and out of a narrow channel as evidenced by Fig. 1 of the instant invention. Therefore, the reference fails to anticipate the claimed invention.

The macromolecules disclosed in Bensimon are attached to a fixed surface. The instant invention claims passing a hybridized DNA complex in a random coil state in a fluid carrier from a reservoir in a microfluidic device through a narrow channel. As shown in Bensimon Fig. 6, one end is attached to a fixed surface preventing the passing of the macromolecule through a narrow channel as claimed by the instant invention. Therefore, the reference fails to teach this limitation.

With respect to Examiners interpretation that Bensimon discloses a "channel" and "reservoir" the claims are interpreted in light of the specification. Clearly the claim defines two distinct features of a microfluidic device. The specification does not limit the claim further but instead, provides information as to the relationship of these two distinctly claimed features as indicated in Fig. 1a. Fig. 1a shows a microfluidic device with a microfluidic channel 10 and a fluid reservoir 20 connected to each end of the channel. The channel 10 and reservoir 20 are shown as distinct features in Fig. 1a. The terms "channel" and "reservoir" as are used both to described the features of Fig. 1a and in Claim 1. Therefore, the specification may provide additional details as to the claimed features of the instant invention. Furthermore, as discussed above the plain meaning of these terms indicates that they are distinct features and not a single element as disclosed by Bensimon.

Bensimon further fails to teach detecting two or more distinct optically distinguishable microparticles on at least two distinct DNA sequence recognition units as claimed by the instant invention as amended.

Bensimon fails to disclose passing a hybridized DNA complex in a fluid carrier from a reservoir in a microfluidic device through a narrow channel. In fact, Bensimon fails to disclose a microfluidic device with a reservoir and a channel as claimed by the instant invention. Bensimon discloses attaching one end of a micromolecule to a fixed surface preventing the passing of the molecule through a channel. Bensimon further fails to teach detecting two or more distinct optically distinguishable microparticles on at least two distinct DNA sequence recognition units as claimed by the instant invention as amended. It is therefore requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 1-6 Under 35 U.S.C. §102(e):

In Section 5 of the Office Action dated September 25, 2006, the Examiner has rejected claims 1-6 under 35 U.S.C. 102(e) as being anticipated by Chan et al (hereinafter referred to as Chan-1; Pre Grant Publication 2003/0059822, 102(e) date 09/18/2001). The Examiner indicates that Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals. The Examiner further indicates that Chan-1 teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to and that Chan-1 teaches determining the sequential order of the labels of the labeled target and thus determining the order of the specific sequence of the target to identify the target DNA molecule. The Examiner states that Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels, that the polymer is preferably a nucleic acid that is genomic DNA and that the unit specific marker can be a nucleic acid probe, or a peptide or polypeptide or peptide-nucleic acids. The Examiner indicates that Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer, and that pressure flow is the preferred driving force of the DNA through such a microchannel recited above. Applicants maintain this rejection as in error as Chan-1 is improperly applied as prior art and fails to disclose all of the claimed limitations of the instant inventions.

Chan-1 provides methods and systems for improved spatial resolution of signal detection, particularly as applied to the analysis of polymers such as biological polymers. The methods and systems comprise differentially tagging polymers in order to increase resolution. The disclose method for analyzing a polymer comprises: a) providing a detection station having a known

detection resolution; b) labeling the polymer with first and second unit specific markers, the first unit specific marker including a first label and the second unit specific marker including a second label distinct from the first label, wherein the first and second unit specific markers are spaced apart on the polymer such that, if the labels were not distinct from each other, they would be separated by a distance less than the detection resolution; c) exposing the polymer labeled as in (b) to the detection station to produce distinct first and second signals arising from the first and second labels; and d) identifying the distinct first and second signals.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of the target molecule to identify the target DNA molecule from its DNA sequence.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. Chan-1 fails to teach passing a hybridized DNA complex in a random coil state in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow as claimed by the instant invention. Applicants direct Examiners attention to paragraph [0127] "the microchannel is a region of constant x-direction shear that maintains the polymer in extended conformation after release from the microposts." By contrast, the instant invention claims an acceleration of fluid flow through the channel. Chan-1

fails to teach all of the claimed limitations of the instant invention therefore, fails to anticipate the instant invention.

Furthermore, 37 C.F.R. 1.131 states "(a) When any claim of an application or a patent under reexamination is rejected, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based. The effective date of a U.S. patent, U.S. patent application publication, or international application publication under PCT Article 21(2) is the earlier of its publication date or date that it is effective as a reference under 35 U.S.C. 102(e). Prior invention may not be established under this section in any country other than the United States, a NAFTA country, or a WTO member country. Prior invention may not be established under this section before December 8, 1993, in a NAFTA country other than the United States, or before January 1, 1996, in a WTO member country other than a NAFTA country."

Chan-1 was filed September 18, 2002, and has priority under 102(e) to September 18, 2001. Applicants conceived the present invention in the U.S. before the applicable 102(e) date of the applied reference, as shown in the previously submitted 37 CFR 1.131 Declaration of co-inventor Zhihao Yang, Tiecheng A. Qiao, Susan J. Muller, and Dorian Liepmann, attached herewith. The invention was first recorded in the notebook of Mr. Yang on June 5, 2001 (European date notation), and was entered into a tracking database (Invention Tracker) and submitted to the legal department of Eastman Kodak Company for preparation of the currently pending patent application in August of 2001. Preparation of the application occurred between August 27, 2001, and the filing date of February 28, 2002, as previously submitted. As shown in the Declaration and documents attached thereto, Applicants date of conception pre-dates the applied references of Chan-1, the Applicants diligently pursued a constructive reduction to practice in the form of the currently pending patent application. Therefore, the Applicants request that the Examiner withdraw the rejection, as Chan-1 fails to anticipate the present invention and the conception of the subject

matter of the rejected claim is prior to the effective date of the reference on which the rejection is based.

Rejection of Claims 1-8 Under 35 U.S.C. §102(e):

In Section 6 of the Office Action dated September 25, 2006 the Examiner has rejected claims 1-8 under 35 U.S.C. 102(e) as being anticipated by Hannah et al (hereinafter referred to as Hannah; U.S. Patent 6,767,731 B2, 102(e) date 08/27/2001).

The Examiner indicates that Hannah teaches a method of sequencing a target nucleic acid comprising hybridization of the target DNA with probes, which can be oligonucleotides and oligonucleotide analogs that are uniquely and detectably labeled, using a microfluidic, device to pass the hybridized nucleic acid through a microchannel to extend it to an approximate linear conformation by hydrodynamic focusing, and detecting the spectral signature of each labeled probe, preferably in sequential order. The Examiner further indicates that Hannah teaches that the labels of multiple probes may be detected in a linear fashion to determine the probe order and identify the target DNA molecule, and that nucleic acid molecules sequenced by this method can be DNA or RNA. The Examiner states that Hannah also teaches that the probe labels can be fluorescent, luminescent, radioactive, phosphorescent, chemiluminescent, enzymatic, spin, electron dense, mass spectroscopic, semiconductor nanostructures, and quantum dots. This rejection is urged as in error as Hannah fails to teach all of the claimed limitations and is misapplied as a prior reference.

Hannah relates to the fields of molecular biology and nucleic acid analysis. In particular, the invention relates to methods, composition and apparatus for electron-induced fluorescent DNA sequencing. Hannah provides an apparatus, compositions and related methods for sequencing a target nucleic acid. In certain embodiments, the apparatus is a microfluidic apparatus comprising an input chamber, microchannel, output chamber and a detection unit that is operatively connected to the microchannel. In preferred embodiments, the methods include hybridizing a target nucleic acid to one or more probe libraries, moving the hybridized target nucleic acid past the detector, and detecting bound probes. Probe libraries may comprise oligonucleotides or oligonucleotide analogs, preferably with each probe uniquely labeled. A linear order of labeled

probes hybridized to the target nucleic acid can be detected and the target nucleic acid sequence deduced. In preferred embodiments, probe labels are detected by analysis of electron- induced fluorescence of probes labeled with conductive polymers.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of the target molecule to identify the target DNA molecule from its DNA sequence.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. Hannah fails to teach attaching an optically distinguishable material to a DNA sequence recognition unit and hybridizing the DNA sequence recognition unit to a target DNA molecule in a random coil state as claimed by the instant invention. The probes disclosed in Hannah are detectable only upon being exposed to an excitation source. In particular an electron beam is used to excite the probes. By contrast, the instant invention claims optically distinguishable material that are colored microparticles. The colored microparticles of the instant invention are optically distinguishable without being excited from an electron beam as taught by Hannah. Therefore, Hannah fails to teach all of the claimed limitations of the instant invention.

Furthermore, 37 C.F.R. 1.131 states "(a) When any claim of an application or a patent under reexamination is rejected, the inventor of the

subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based. The effective date of a U.S. patent, U.S. patent application publication, or international application publication under PCT Article 21(2) is the earlier of its publication date or date that it is effective as a reference under 35 U.S.C. 102(e). Prior invention may not be established under this section in any country other than the United States, a NAFTA country, or a WTO member country. Prior invention may not be established under this section before December 8, 1993, in a NAFTA country other than the United States, or before January 1, 1996, in a WTO member country other than a NAFTA country."

Hannah et al. was first filed in the United States August 27, 2001. Applicants conceived the present invention in the U.S. before the applicable 102(e) date of the applied reference, as shown in the previously submitted 37 CFR 1.131 Declaration of co-inventor Zhihao Yang, Tiecheng A. Qiao, Susan J. Muller, and Dorian Liepmann, attached herewith. The invention was first recorded in the notebook of Mr. Yang on June 5, 2001 (European date notation), and was entered into a tracking database (Invention Tracker) and submitted to the legal department of Eastman Kodak Company for preparation of the currently pending patent application in August of 2001. Preparation of the application occurred between August 27, 2001, and the filing date of February 28, 2002, as previously submitted. As shown in the Declaration and documents attached thereto, Applicants date of conception pre-dates the applied references of Hannah, the Applicants diligently pursued a constructive reduction to practice in the form of the currently pending patent application. Therefore, the Applicants request that the Examiner withdraw the rejection, as Hannah does not anticipate the present invention.

Sufficiency of Declaration Filed Under 37 C.F.R. §1.131:

In Section 7 of the Office Action dated September 25, 2006 the Examiner indicates that the declaration filed under 37 C.F.R. §1.131 has been thoroughly reviewed but was not found persuasive to overcome the rejections over

Chan-1 and Hannah. The Examiner notes that several limitations of the instant claims are not disclosed by "notebook page 154". With regard to claim 1, part c), the "notebook page 154" does not disclose any teachings of a "reservoir" from which the DNA is passed from. In addition claim 1, part c) recites passing the DNA "from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear confirmation". The 'notebook page 154' does not teach how the stretching of the DNA relates to the "acceleration of fluid flow through said channel" recited in instant claim 1. The Examiner indicates that the mere reference, on "notebook page 154", of "as shown in Berkeley" is not considered specific enough to point to the limitations provided in the article "Effect of flow on complex Biological macromolecules in microfluidic devices," by Polly S Shrewsbury, Susan J Muller and Dorian Liepmann published in 2001 in Biomedical Microdevices, 3:3, 225-238 by Kluwer Academic Publishers. The Examiner states that phrase "as shown in Berkeley" recited in "notebook page 154", part c) is given no consideration with regard to the applicant's response regarding the Biomedical Microdevices article because it remains unclear how such recitation relates to the invention or the provided article. The Examiner also notes that "notebook page 154" is provide with a date of Jun 5, 2001, the publication information for the article (vol.3 no.3) appears to indicate a publication date of September 2001. The Examiner further indicates that even upon review of the provided Biomedical Microdevices article, the article does not address the further limitations of the claims such as microparticles having different shapes (claim 3), nanocrystals (claim 4), peptide nucleic acids (claim 5), or protein scaffolds or synthetic molecular moiety (claim 6); and while the article teaches a channel with the particular dimensions of 300 um wide x 60 um deep, the reference does not teach a range of widths or depths as recited in claims 7 and 8. This rejection is respectfully urged in error.

The previously submitted Declarations provide "notebook page 154" which discloses the steps of: a) attaching different oligonucleotides with different colored beads, b) hybridizing the labeled oligonucleotides with unknown DNA molecule, c) stretching the DNA molecules from random coil to linear confirmation under microscopy by a microfluidic device as shown in Berkeley, d) and recording the order of colored beads to determine the species of DNA.

"Berkley" refers to the article "Effect of Flow on Complex Biological Macromolecules in Microfluidic Devices", as indicated in the previously submitted Declaration of co-inventor Zhihao Yang, Tiecheng A. Qiao, Susan J. Muller, and Dorian Liepmann. The article, previously submitted, discloses a "reservoir" from which the DNA is passed, and teaches how the stretching of the DNA relates to the "acceleration of fluid flow through said channel" recited in instant claim 1.

The inventors signed the Declaration under 37 CFR. §1.131 dated June 20, 2006 stating that the reference on the notebook page "as shown in Berkeley" refers to a published article "Effect of Flow on Complex Biological Macromolecules in Microfluidic Devices," by Polly S. Shrewsbury, Susan J. Muller, and Dorian Liepmann and published in 2001 in Biomedical Microdevices,3:3, 225-238 by Kluwer Academic Publishers. The inventors acknowledged that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon. Additionally, an accompanying exhibit need not support all claimed limitations, provided that any missing limitation is supported by the declaration itself. *Ex parte Ovshinsky*, 10 USPQ2d 1075 (Bd. Pat. App. & Inter. 1989). The declaration states that the claimed invention was conceived in the U.S. prior to the references to Chan-1 and Hannah. The Declaration in combination with notebook page 154 is sufficient to show conception prior to Chan-1 and Hannah. The notebook page specifically discloses stretching the DNA molecules by use of a microfluidic device and the inventors state that the claimed invention was conceived prior to the references. Furthermore, the Declaration explicitly states that the reference "as shown in Berkeley" on the notebook page refers to the Biomedical Microdevices article. With respect to the difference in dates between the notebook page and the publication date of the article, it is understood that articles are not contemporaneously published upon submission, and that an article may publish after it has been actually written. It should be noted that multiple inventors are also co-authors of the article and the reference to the Berkeley article refers to the Biomedical Microdevices article previously submitted. The authors of the Biomedical Microdevices article are all members of the University of

California, Berkeley; hence the notation "as shown in Berkeley" is understood by the inventors. The Examiner contends that the mere reference on the notebook page "as shown in Berkeley" is not specific enough to point to the Biomedical Microdevices article. However, Examiner must account for the signed declaration, which explicitly clarifies that the inventors understood that the phrase "as shown in Berkeley" refers to the Biomedical Microdevices article. The Declaration, in combination with the notebook page and the Biomedical Microdevices article, are sufficient to show conception prior to the references.

Therefore, Applicants have established that the claimed invention was conceived prior to the US filing date of Hannah or Chan-1. Applicants respectfully request that these rejections be reconsidered and withdrawn in light of the Declarations and evidence previously submitted.

Rejection of Claims 1 and 5-8 Under 35 U.S.C. §102(e):

In Section 8 of the Office Action dated September 25, 2006, the Examiner has rejected claims 1 and 5-8 under 35 U.S.C. 102(e) as being anticipated by Chan et al PCT/US00/22253 (WO 01/13088 publication date 02/22/2001, herein referred to as Chan-2).

The Examiner indicates that Chan-2 teaches methods comprising extrinsically labeling a target nucleic acid sequence using an oligonucleotide to which a label such as a fluorescent dye is attached, a labeled oligonucleotide can be hybridized to a target DNA to "mark" a specific target sequence in the target, the target DNA may be "marked" when it is in a random coil state, passing the labeled target DNA through a channel in a fluid carrier to cause the target label complex to extend into a linear conformation, and that the effect of accelerated fluid flow causes the target DNA to extend. The Examiner further indicates that Chan-2 teaches the detection of the labels on the target DNA along the length of the target, and that the method can be used to analyze polymers to determine polymer sequence, which is a determination of the sequential order of the labels of the DNA sequence recognition unit thereby identifying the target DNA molecule. This rejection is respectfully traversed.

Chan-2 relates to the general field of polymer characterization. More particularly, the reference relates to the use of structures to stretch a polymer or to select a polymer on the basis of length in a chip. The reference provides

structures and methods that allow polymers of any length, including nucleic acids containing entire genomes, to be stretched into a long, linear conformation for further analysis. The reference also provides structures and methods for selecting and stretching polymers based on their lengths. Polymers are loaded into a device and run through the structures. Stretching is achieved by, e.g., applying shear forces as the polymer passes through the structures, placing obstacles in the path of the polymer, or a combination thereof. Since multiple molecules may be stretched in succession, extremely high throughput screening, e.g., screening of more than one molecule per second, is achieved.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of the target molecule to identify the target DNA molecule from its DNA sequence.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. Chan-2 fails to disclose attaching microparticles to a DNA sequence recognition unit as claimed by the instant invention, as amended. This is further stated in Section 12 of the Office Action dated September 25, 2006. Furthermore, Chan-2 fails to disclose utilizing at least 2 distinct DNA sequence recognition units as claimed by the instant invention.

As Chan-2 fails to disclose all of the claimed limitations of the instant invention it is respectfully requested that this rejection be reconsidered and withdrawn. Additionally, the response to remarks in Section 9 of the Office action dated September 25, 2006 are not relevant to the present invention as amended.

Rejection of Claims 7 and 8 Under 35 U.S.C. §103(a):

In Section 10 of the Office Action dated September 25, 2006, the Examiner has rejected claims 7 and 8 under 35 U.S.C. 103(a) as being unpatentable over Chan-1, in view of Chan-2 et al (hereinafter referred to as Chan-2; PCT/USOO/22253, International Publication Number WO 01/13088 Al, International Publication Date 02/22/2001).

The Examiner indicates that Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals, Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to, Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels, Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA, and that the unit specific marker can be a nucleic acid probe, Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a fluorescent molecule, a radioisotope, an enzyme, a biotin molecule, an avidin molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a micro bead, a protein, a peptide, a nucleic acid, a carbohydrate, an antigen, an antibody, etc., Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system, Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce

a signal or polymer dependent impulse, by movement of the marker and the station relative to one another, Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer, Chan-1 teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1), with regard to instant claim 1.d) reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex, ...", the recitation is interpreted as detecting one or more optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Chan-1, and Chan-1 teaches stretching DNA by passing the DNA through a microchannel. The Examiner continues that, although Chan-1 is silent with respect to the width or depth of the channel, Chan-2 teaches that a channel with 1 μm depth, 1 mm length, and a shear rate of 0.25/s gives a force of approximately 0.25 pN, which the inventors have verified experimentally is adequate to stretch DNA, making it prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Chan-1 with the device of Chan-2 because Chan-2 specifically teaches a device for performing the method of Chan-1 and the ordinary artisan would have been motivated to use the device of Chan-2 because Chan-1, while generally teaching a method of stretching DNA with a microfluidic device, is silent with regard to the specific structure and dimensions of the device, the device, with its specific dimensions, taught by Chan-2 functions to stretch DNA as taught by Chan-1, the ordinary artisan would be motivated to use the device of Chan-2 in the method of Chan1 because Chan-1 teaches to stretch DNA by passing the DNA through a microchannel, but no specific structure or dimensions of the microchannel are recited.

Chan-1 provides methods and systems for improved spatial resolution of signal detection, particularly as applied to the analysis of polymers such as biological polymers. The methods and systems comprise differentially tagging polymers in order to increase resolution. The disclose method for analyzing a polymer comprises: a) providing a detection station having a known

detection resolution; b) labeling the polymer with first and second unit specific markers, the first unit specific marker including a first label and the second unit specific marker including a second label distinct from the first label, wherein the first and second unit specific markers are spaced apart on the polymer such that, if the labels were not distinct from each other, they would be separated by a distance less than the detection resolution; c) exposing the polymer labeled as in (b) to the detection station to produce distinct first and second signals arising from the first and second labels; and d) identifying the distinct first and second signals.

Chan-2 relates to the general field of polymer characterization. More particularly, the invention relates to the use of structures to stretch a polymer or to select a polymer on the basis of length in a chip. The invention provides structures and methods that allow polymers of any length, including nucleic acids containing entire genomes, to be stretched into a long, linear conformation for further analysis. The invention also provides structures and methods for selecting and stretching polymers based on their lengths. Polymers are loaded into a device and run through the structures. Stretching is achieved by, e.g., applying shear forces as the polymer passes through the structures, placing obstacles in the path of the polymer, or a combination thereof. Since multiple molecules may be stretched in succession, extremely high throughput screening, e.g., screening of more than one molecule per second, is achieved.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of

the target molecule to identify the target DNA molecule from its DNA sequence.

37 CFR 1.131 states "(a) When any claim of an application or a patent under reexamination is rejected, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based. The effective date of a U.S. patent, U.S. patent application publication, or international application publication under PCT Article 21(2) is the earlier of its publication date or date that it is effective as a reference under 35 U.S.C. 102(e). Prior invention may not be established under this section in any country other than the United States, a NAFTA country, or a WTO member country. Prior invention may not be established under this section before December 8, 1993, in a NAFTA country other than the United States, or before January 1, 1996, in a WTO member country other than a NAFTA country."

As discussed above, Chan-1 was filed September 18, 2002, and has priority under 102(e) to September 18, 2001. As shown in the previously submitted Declarations and documents attached thereto, Applicants date of conception pre-dates the applied references of Chan-1, and Applicants diligently pursued a constructive reduction to practice in the form of the currently pending patent application, removing Chan-1 as a reference. Chan-2 does not teach or suggest all the features of the claimed invention. Therefore, the Applicants request that the Examiner reconsider and withdraw the rejection.

In Section 11 of the Office Action dated September 25, 2006, the Examiner indicates that the declaration does not overcome the rejection by Chan-1 with regard to claims 1-6. With regard to the further limitations of claims 7 and 8, it is noted that the Declaration does not provide teachings encompassing the range of dimensions of the channel of the microfluidic device.

As discussed above all the exhibits need not support all claimed limitations, provided that any missing limitation is supported by the declaration itself. Furthermore, as discussed above, the Declaration and exhibits are sufficient

to establish conception prior to Chan-1. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 2-4 Under 35 U.S.C. §103(a):

In Section 12 of the Office Action dated September 25, 2006, the Examiner has rejected claims 2-4 under 35 U.S.C. 103(a) as being unpatentable over Chan et al PCT/USOO/22253 (WO 01/13088 publication date 02/22/2001, herein referred to as Chan-2) in view of Bensimon et al (U.S. Patent 6,054,327).

The Examiner indicates that as discussed in Section 8 of the Office Action dated September 25, 2006, Chan-2 teaches a method for single molecule identification of a target DNA comprising all of the limitations of claim 1, from which rejected claims 2-4 depend. The Examiner states that Chan-2 does not specifically teach the labeling of oligonucleotide probes with microparticles. The Examiner states that Bensimon teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads. The Examiner indicates that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the oligonucleotide labeling techniques taught by Bensimon et al to analyze oligonucleotide probes hybridized to target DNA molecules in the methods of Chan-2. One would have been motivated to use the techniques of Bensimon based on the assertion that such methods are suitable for the detection of probes hybridized to a single target DNA molecule stretched into a linearized conformation. This rejection is respectfully traversed.

Bensimon discloses a method for aligning macromolecules such as polymers or macromolecules with biological activity, especially DNA, or proteins and also relates to the application of this method in processes for detecting, for measuring intramolecular distance, for separating and/or for assaying a macromolecule in a sample. Macromolecules such as nucleic acids, proteins, lipids or polysaccharides are aligned on a support surface by passing the macromolecules through a meniscus of a solvent containing the macromolecules. The meniscus may be that of a solvent between two surfaces at an interface of the solvent with air. One end of a macromolecule is attached to one surface, which may be a glass surface, and another end is free. The meniscus is moved relative to the surface to which the end is attached such as by evaporating the solvent or by moving the surface. As the macromolecule passes through the meniscus, the

macromolecule aligns on the surface perpendicular to the meniscus. This method may be used in assaying, measuring intramolecular distance and/or separating of macromolecules.

Chan-2 relates to the general field of polymer characterization. More particularly, the invention relates to the use of structures to stretch a polymer or to select a polymer on the basis of length in a chip. The invention provides structures and methods that allow polymers of any length, including nucleic acids containing entire genomes, to be stretched into a long, linear conformation for further analysis. The invention also provides structures and methods for selecting and stretching polymers based on their lengths. Polymers are loaded into a device and run through the structures. Stretching is achieved by, e.g., applying shear forces as the polymer passes through the structures, placing obstacles in the path of the polymer, or a combination thereof. Since multiple molecules may be stretched in succession, extremely high throughput screening, e.g., screening of more than one molecule per second, is achieved.

The present invention relates to a method for single molecule identification of a target DNA molecule in a random coil state by attaching an optically distinguishable material to a DNA sequence recognition unit, which is specific to a particular sequence of DNA, hybridizing at least two distinct optically distinguished DNA sequence recognition unit to a target DNA molecule in a random coil state, passing the target DNA molecule, now hybridized with at least two distinct optically distinguished DNA sequence recognition unit, in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing the hybridized DNA complex to extend into a substantially linear configuration, detecting the optically distinguishable material in a sequential manner, determining, from this sequence of optically distinguished material, the sequential order of the specific DNA sequences of the target molecule to identify the target DNA molecule from its DNA sequence.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a

reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

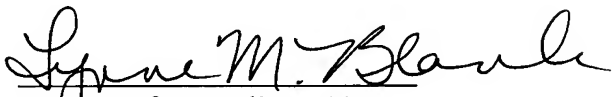
As discussed above, Claim 1 reads "passing said hybridized DNA complex in a random coil state in a fluid carrier from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" MPEP 2111.01 states that "the words of a claim must be given their "plain meaning" unless they are defined in the specification." This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In addition, MPEP 2111.01 continues that ""Plain meaning" refers to the ordinary and customary meaning given to the term by those of ordinary skill in the art" and "It is the use of the words in the context of the written description and customarily by those skilled in the relevant art that accurately reflects both the "ordinary" and the "customary" meaning of the terms in the claims. Ferguson Beauregard/Logic Controls v. Mega Systems, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003). As discussed above, Bensimon fails to disclose passing a hybridized DNA complex from a reservoir in a microfluidic device through a narrow channel as claimed by the instant invention. Furthermore, the specification supports the definition of "through" as the movement of the hybridized DNA complex in one side of the channel and out the other side of the channel. See Fig. 1a and 1c (A, B, C, D, E, F). Also as discussed above the normal reading of the claim would indicate that the entire complex passes in one end and out the other of the narrow channel. Fig. 1a and 1c also clarify that the entire complex passes through the channel.

Neither Bensimon et al. nor Chan-2 disclose or suggest attaching colored microparticles to a DNA sequence recognition unit and passing the hybridized DNA complex as presently claimed from a reservoir in a microfluidic device through a channel to sequence the target DNA molecule, thereby allowing identification of the target molecule. Furthermore, neither reference discloses detecting two or more distinct optically distinguishable microparticles on at least two distinct DNA sequence recognition units as claimed by the instant invention as amended. Since neither reference discloses all of the claimed limitations, the

combined references fail to provide a likelihood of success that one would be able to sequence the target DNA molecule, thereby allowing identification of the target molecule. Since neither Bensimon nor Chan-2 disclose or suggest passing a hybridized DNA complex as presently claimed from a reservoir in a microfluidic device through a channel to sequence the target DNA molecule, thereby allowing identification of the target molecule, the references fail to disclose all the present claim limitations. Therefore, since the combination of the references fail to produce the presently claimed invention, fail to provide any likelihood of success and fail to disclose all the present claims limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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